Oral pathology in oncological patients. Effects of chemotherapy and radiotherapy. Preventive and treatment strategies
Evidence-Based Management Strategies for Oral Complication from Cancer Treatment

- The definition, prevalence and management strategies based on the literature are presented for the following oral complications:
  - Bisphosphonate Osteonecrosis (BON)
  - Dysgeusia
  - Oral Fungal Infection
  - Oral Viral Infection
  - Dental Disease
  - Osteoradionecrosis (ORN)
  - Trismus
  - Oral Pain
  - Xerostomia
Bisphosphonate Osteonecrosis (BON)

- **Definition**

  BON is defined as the presence of necrotic bone anywhere in the oral cavity of an individual on bisphosphonate therapy with no history of radiation of the head and neck.
Bisphosphonate Osteonecrosis (BON)

- **Prevalence**
  - Mean weighted prevalence of BON for all studies = 6.1%
  - Epidemiological studies = 1.2%

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Bisphosphonate Osteonecrosis (BON)

• Management
  - The types of procedures used in published studies have included the following:
    - Antibiotics (59.7%)
    - Simple bone sequestrectomy (23.4%)
    - Bisphosphonate stopped (16.1%)
    - Conservative therapy (15.2%)
    - Extensive surgical debridement (12.8%)
    - Unspecified surgery with antibiotics (6.8%)
    - IV antibiotics with hospitalization (0.6%)

• The response to therapy has been poorly reported with 47% of responses not clearly specified in published studies. BON completely resolved in only 12% of cases, while 33% remained stable and 7% progressed.

• Due to flaws in published studies and the paucity of data regarding management strategies, no guideline is possible regarding prevention or treatment strategies.
Dysgeusia

- **Definition**
  
  Dysgeusia is an abnormal or impaired sense of taste, an unpleasant alteration of taste sensation, or a distortion or perversion of the sense of taste.

- **Prevalence**
  
  Mean weighted prevalence of dysgeusia
  
  - Chemotherapy only = 56.3%
  - Radiotherapy only = 66.5%
  - Combined RT and CT = 76%
Dysgeusia

- **Management**

  Dietary and educational counseling

  - Suggestion to use counseling for the prevention of dysgeusia.
Oral Fungal Infection

- Definition

Oral infection of fungal etiology. Oral candidiasis accounts for the majority of oral fungal infections, with clinical presentations including pseudomembranous candidiasis (thrush), erythematous candidiasis (red appearance), hyperplastic candidiasis (white tissue overgrowth) and angular cheilitis (redness at corners of mouth).
Oral Fungal Infection

- Weighted prevalence of oral colonization with fungal organisms
  - Before cancer treatment = 48.2%
  - During cancer treatment = 72.2%
  - After cancer treatment = 70.1%.

- Weighted prevalence of oral fungal colonization by cancer treatment
  - During chemotherapy = 72.8%
  - During radiation therapy = 74.5%
pseudomembranous candidiasis
Management

- **Topical antifungal agents.** There is inconsistency in the efficacy of topical antifungal agents as antifungal prophylaxis for patients receiving cancer therapy. No recommendation possible.

- **Systemic antifungal agents.** Recommend the use of systemic fluconazole for the prevention of oral candidiasis in patients receiving cancer therapy.
  - Fluconazole
Oral Viral Infection

• Definition

Oral and perioral manifestations of viral infections; often a local component of a systemic disease.

Oral and perioral viral infections are most commonly associated with herpesviruses, particularly herpes simplex virus (HSV) numerous studies addressed this issue. Information about other oral viral infections (cytomegalovirus (CMV), varicella zoster virus (VZV), Epstein-Barr virus (EBV)) is sparse.
Oral Viral Infection

- Prevalence of HSV oral and perioral infection:
  - Weighted prevalence in patients treated with chemotherapy for hematologic malignancies
    - Patients with oral ulcerations – 49.8%
  - Weighted prevalence in patients treated with radiotherapy
    - Patients with radiotherapy only - sampling oral ulcerations = 0%
    - Patients with radiotherapy and adjunctive chemotherapy - sampling oral ulcerations = 43.2%
Management

Both acyclovir and valacyclovir are recommended for the prevention of HSV infection.

Prevention may be achieved with acyclovir dose of 800 mg/day or with valacyclovir dose of 500-1000 mg/day.

There are no studies in the literature about protocols for anti-viral treatment.

The presence of HSV reactivation was similar for acyclovir and valacyclovir; However, there may be superiority of valacyclovir compared to acyclovir in respect to toxicity and to cost (depends on the route of administration of acyclovir—PO or IV).
Dental Diseases

- **Definition:**

  Dental caries involves decay of the tooth structure, gingival disease is caused by inflammation of the gum tissue surrounding the tooth and a dental infection/abscess is a bacterial infection resulting for a necrotic pulp or from diseased bone/tissue structure surrounding a tooth.
Dental Diseases

• Prevalence
  – Weighted prevalence for dental caries in patients treated with cancer therapy
    • All studies = 28.1%
    • Chemotherapy only = 37.3%
    • Post-radiotherapy = 24%
    • Post chemotherapy and radiotherapy = 21.4%
  – Weighted prevalence of severe gingivitis in patients undergoing chemotherapy = 20.3%
  – Weighted prevalence of dental infection/abscess in patients undergoing chemotherapy = 5.8%
• Management

- Recommend the use of fluoride to prevent dental caries in patients who are post-radiotherapy. Studies indicated fluoride works regardless of the type of delivery method.

- Recommend the use of chlorhexidine to improve oral hygiene, although potential side effects of tooth staining, increased calculus, and taste changes need to be taken into account.

- Suggest the use of resin-modified glass ionomer, composite resin and not a conventional glass ionomer restoration in patients who have been treated with radiotherapy.

- No guideline possible due to the lack of well designed studies regarding the benefits of various types of toothpaste and pre-cancer therapy dental intervention.
Osteoradionecrosis

• Definition

ORN is characterized by a nonhealing area of exposed mandibular and maxillary bone of at least 6 months duration in a patient who has been treated with radiation therapy (RT) for cancer.
Osteoradionecrosis

- **Prevalence**
  - Weighted prevalence in *conventional RT* = 7.4%
  - Weighted prevalence in intensity modulated RT = 5.2%
  - Weighted prevalence in RT and chemotherapy = 6.8%
  - Weighted prevalence in brachytherapy = 5.3%
  - **Note:** The majority of cases involve the mandible.
Management

- Practitioners should utilize their clinical experience and expertise in determining optimal management for their patients relative to ORN of the mandible or the maxilla.

- No guideline is possible regarding the use of prophylactic HBO (Hyperbaric oxygen therapy) therapy for the prevention of ORN in patients requiring post-RT dental extractions.

- The use of single therapy HBO therapy for the treatment of ORN is NOT recommended.

- No guidelines possible for other prevention and treatment strategies for ORN.
Trismus

- Definition

Trismus is defined as the tonic contraction of the muscles of mastication and results in a limited ability to open the mouth. This has been associated with radiotherapy (RT) to the temporomandibular joint and muscles of mastication.
Trismus

- Prevalence
  - Weighted prevalence for conventional RT = 25.4%
  - Weighted prevalence for intensity modulated RT = 5%
  - Weighted prevalence for combined RT and chemotherapy = 30.7%
Trismus

- **Management**
  - Suggestion that Therabite® System may be effective in the reduction of RT-induced trismus.
  - No guideline is possible regarding the use of physiotherapy in the prevention of RT-induced trismus, although may be beneficial in overall trismus management.
  - No guideline possible regarding use of Dynasplint® Trismus System in the reduction of RT-induced trismus, although may have some benefit for reduction of contracture of the muscles of mastication.
Oral Pain

- **Definition**
  
  Cancer-associated pain in the orofacial region is common and can be directly related to the malignancy or is a consequence of cancer therapy.

- **Prevalence**
  
  - Pain is common in patients with HNC and reported by approximately half of patients prior to cancer therapy, 81% during therapy, 70% at the end of therapy and still 36% at 6 months post-treatment.

  - VAS Pain level (0-100) in Head and Neck Cancer patients
    
    - Pre-treatment = 12/100
    - Immediately post-tx = 33/100
    - One month post-tx = 20/100
Effects of radiotherapy and chemotherapy on oral mucosa

- Normal epithelium
- Radiotherapy and chemotherapy initiate cell damage
- The mucosa is damaged prior to the appearance of redness or sores
- Mucosal damage progresses to ulceration and opens a portal to potential infection
- After a period of 2-3 weeks following the initial insult, the mucosa undergoes a healing process
Signs and symptoms of mucositis include:

- Red, shiny, or swollen mouth and gums
- Blood in the mouth
- Sores in the mouth or on the gums or tongue
- Soreness or pain in the mouth or throat
- Difficulty swallowing or talking
- Feeling of dryness, mild burning, or pain when eating food
- Soft, whitish patches or pus in the mouth or on the tongue
- Increased mucus or thicker saliva in the mouth

An extreme case of the condition is called confluent mucositis. In a worst case, the mucous membrane of the patient’s entire mouth and tongue can be coated by a white mucus coating that is up to a millimeter thick. The combination of mucus, excess saliva and pain can make it difficult or even impossible to eat.
mucositis
Management

1. Clinical trials for the treatment of oral pain in cancer patients is often a secondary outcome with mucositis the primary outcome.

2. The treatment of mucositis is symptomatic:
   - In mild cases water ice or ice chips may help numb the area.
   - Topical pain relievers include lidocaine and benzocaine. Corticosteroids such as prednisone may be effective.
   - Benadryl® elixir, lozenges and analgesics may help reduce mouth pain.
   - Swish diluted milk of magnesia,
   - Oral Balance is a dental gel that moistens the mouth while sores are healing and also has enzymes that help control oral bacteria.
   - Orabase B (OTC) is an adhesive paste with a topical anesthetic (benzocaine) that may be helpful.
Biotène Oral Balance Gel
For Moderate to Severe Dry Mouth
Long Lasting Symptom Relief

Net WT 1.5 OZ (42g)

Orabase
Maximum Strength Oral Pain Reliever
20% Benzocaine
Net WT 0.42 OZ (11.9 g)

Colgate Orabase
FAST RELIEF for CANKER & MOUTH SORES
Maximum strength relief for:
- Canker sores
- Cheek bites
- Toothbrush irritations
- Denture irritations
- Orthodontic irritations

#1 Recommended by Pharmacists
Soothing Mint
ALCOHOL FREE

ALCOHOL FREE
Salivary gland hypofunction and xerostomia

- **Definition**

  Salivary gland hypofunction is a decrease in salivary secretion, with pathological low saliva secretion as ≤ 0.1 ml/min for unstimulated whole salivary flow and ≤ 0.5 ml/min for stimulated whole salivary flow.

  Xerostomia is defined as the subjective complaint of dry mouth.
Prevalence

- Weighted prevalence of xerostomia in head and neck cancer patients by type of radiation therapy (RT)
  - All studies
    - Pre-tx = 6%
    - During RT = 93%
    - 1-3 months post-RT = 74%
    - 3-6 months post-RT = 79%
    - 6-12 months post-RT = 83%
    - 1-2 years post-RT = 78%
    - > 2 years post-RT = 85%
  - Conventional RT
    - Pre-tx = 10%
    - During RT = 81%
    - 1-3 months post-RT = 71%
    - 3-6 months post-RT = 83%
    - 6-12 months post-RT = 72%
    - 1-2 years post-RT = 84%
    - > 2 years post-RT = 91%
Salivary gland hypofunction and xerostomia

- Weighted prevalence of xerostomia in head and neck cancer patients by type of radiation therapy (RT)
  - Intensity-modulated radiation therapy (IMRT)
    - Pre-tx = 12%
    - During RT = 100%
    - 1-3 months post-RT = 89%
    - 3-6 months post-RT = 73%
    - 6-12 months post-RT = 90%
    - 1-2 years post-RT = 66%
    - > 2 years post-RT = 68%
Unstimulated and stimulated whole saliva flow changes during and after radiotherapy in the head and neck region.

Saliva Check test
CRT test for Streptococcus mutans and Lactobacillus
Salivary gland hypofunction and xerostomia

- Management
  - The panel recommends the use of parotid sparing IMRT for prevention of salivary gland hypofunction and xerostomia in head and neck cancer patients.
  - No guideline possible for use of amifostine to prevent xerostomia during RT for head and neck cancer due to lack of consensus on the interpretation of existing evidence.
  - The panel recommends the use of oral pilocarpine following radiation therapy in head and neck cancer patients for improvement of xerostomia. The improvement of salivary gland hypofunction may be limited.
Salivary gland hypofunction and xerostomia

- **Management**
  - No guideline possible for use of gustatory and masticatory stimulation due to little evidence on which to base a guideline since this has been sparsely addressed specifically for patients suffering from xerostomia induced by cancer therapies.
  - The panel recommends the use of oral mucosal lubricants/saliva substitutes for short-term improvement of xerostomia following radiation therapy in head and neck cancer patients.
  - The panel suggests that the obtained level of sparing by submandibular salivary gland transfer might be of clinical significance.
  - The panel suggests the use of acupuncture to stimulate salivary gland secretion and to alleviate xerostomia.
  - No guideline possible for hyperbaric oxygen treatment of xerostomia due to no evidence on which to base a guideline.
saliva substitutes